

## SEQUENCE LISTING

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caa tgg gtg Gln Trp Val							528
atc tta ccg Ile Leu Pro		Ser Thr G					576
cgt gtt act Arg Val Thr 195							624
ctc tcc agc Leu Ser Ser 210							672
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caa tgg gtg cgt cag Gln Trp Val Arg Gln 165	Ala Pro Gly Gln			

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35 40 45  Leu Ile Tyr Gly Ala Thr Asn Leu Ala Asp Gly Val Pro Ser Arg Phe	

Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Gly

100 105 110

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gln Val 115 120 125

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val 130 135 140

Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Ser Asn Tyr Trp Ile 145 150 155 160

Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Glu 165 170 175

Ile Leu Pro Gly Ser Gly Ser Thr Glu Tyr Ala Gln Lys Phe Gln Gly 180 185 190

Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr Met Glu 195 200 205

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg 210 215 220

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<220>

<221> CDS

<222> (1)..(744)

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48

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					tat Tyr									144
					acg Thr									192
					gga Gly 70	_	-		_		_	_	_	240
					gct Ala									288
					cag Gln									336
					ggc Gly									384
					ggc Gly									432
					gct Ala 150									480
					gcc Ala									528
					ggt Gly									576
					cgt Arg									624
					tcg Ser									672
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Gly Thr Leu Val Thr Val Ser Ser 245

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Gly Ala Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu 35 40 45

Leu Ile Tyr Gly Ala Thr Asn Leu Ala Asp Gly Val Pro Ser Arg Phe 50 55 60

Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu 65 70 75 80

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Asn Val Leu Asn Thr 85 90 95

Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Gly 100 105 110

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gln Val 115 120 125

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val 130 135 140

Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Ser Asn Tyr Trp Ile 145 150 155 160

Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Glu 165 170 175

Ile Leu Pro Gly Ser Gly Ser Thr Glu Tyr Thr Glu Asn Phe Lys Asp 180 185 Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr Met Glu 195 200 205 Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg 210 220 Tyr Phe Phe Gly Ser Ser Pro Asn Trp Tyr Phe Asp Val Trp Gly Gln 235 225 Gly Thr Leu Val Thr Val Ser Ser 245 <210> 7 <211> 747 <212> DNA <213> Artificial <220> <223> Humanized antibody <220> <221> CDS (1)...(744)<222> <400> 7 atg gcc gat atc cag atg acc cag tcc ccg tcc tcc ctg tcc gcc tct 48 Met Ala Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser 96 gtg ggc gat agg gtc acc atc acc tgc cgt gct agc gaa aac atc tat Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr 20 25 144 qqc qcq ctq aac tqq tat caa caq aaa cct ggg aaa gct ccg aag ctt Gly Ala Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu 35 192 ctg att tac ggt gcg acg aac ctg gca gat gga gtc cct tct cgc ttc Leu Ile Tyr Gly Ala Thr Asn Leu Ala Asp Gly Val Pro Ser Arg Phe 50 tet gga tee gge tee gga acg gat tte act etg ace ate age agt etg 240 Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu 75 80 65 70 cag cct gaa gac ttc gct acg tat tac tgt cag aac gtt tta aat act 288

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Asn Val Leu Asn Thr

90 85 95 ccg ttg act ttc gga cag ggt acc aag gtg gaa ata aaa cgt act ggc 336 Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Gly 105 100 ggt ggt ggt tct ggt ggc ggt gga tct ggt ggc ggt tct caa gtc 384 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gln Val 120 115 432 caa ctq qtq caa tcc qqc qcc qag qtc aag aag cca ggg gcc tca gtc Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val 130 135 480 aaa gtg tcc tgt aaa gct agc ggc tat att ttt tct aat tat tgg att Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Ser Asn Tyr Trp Ile 145 caa tgg gtg cgt cag gcc ccc ggg cag ggc ctg gaa tgg atg ggt gag 528 Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Glu atc tta ccq ggc tct ggt agc acc gaa tat gcc caa aaa ttc cag ggc 576 Ile Leu Pro Gly Ser Gly Ser Thr Glu Tyr Ala Gln Lys Phe Gln Gly 180 185 cqt qtt act atq acq cqt gac act tcg act agt aca gta tac atg gag 624 Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr Met Glu 200 205 195 ctc tcc agc ctg cga tcg gag gac acg gcc gtc tat tat tgc gcg cgt 672 Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg 210 215 220 720 tat ttt ttt ggt tct agc ccg aat tgg tat ttt gat gtt tgg ggt caa Tyr Phe Phe Gly Ser Ser Pro Asn Trp Tyr Phe Asp Val Trp Gly Gln 225 230 235 240 747 gga acc ctg gtc act gtc tcg agc tga Gly Thr Leu Val Thr Val Ser Ser 245 <210> 8 <211> 248 <212> PRT <213> Artificial <220> Synthetic Construct <400> 8 Met Ala Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser 10 15

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Gly Thr Leu Val Thr Val Ser Ser

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                                                                       96
gtg ggc gat agg gtc acc atc acc tgc ggc gcc agc gaa aac atc tat
Val Gly Asp Arg Val Thr Ile Thr Cys Gly Ala Ser Glu Asn Ile Tyr
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                                                                      144
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Gly Ala Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu
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ctg att tac ggt gcg acg agc ctg cag tct gga gtc cct tct cgc ttc
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Leu Ile Tyr Gly Ala Thr Ser Leu Gln Ser Gly Val Pro Ser Arg Phe
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Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu
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cag cct gaa gac ttc gct acg tat tac tgt cag aac gtt tta aat act
Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Asn Val Leu Asn Thr
ccq ttq act ttc gga cag ggt acc aag gtg gaa ata aaa cgt act ggc
                                                                      336
Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Gly
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            100
ggt ggt tct ggt ggc ggt gga tct ggt ggc ggt tct caa gtc
                                                                      384
Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gln Val
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Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val
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145
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cgt gtt act Arg Val Thr 195												624
ctc tcc agc Leu Ser Ser 210			Asp									672
tat ttt ttt Tyr Phe Phe 225					Tyr :							720
gga acc ctg Gly Thr Leu	_		-	tga								747
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	gcg Ala															144
_	att Ile 50				_	_										192
	gga Gly					-	-			_						240
	cct Pro															288
_	ttg Leu				_			_		_			_			336
	ggt Gly															384
	ctg Leu 130					_		_	_				-			432
	gtg Val															480
	tgg Trp															528
	tta Leu															576
	gtt Val															624
	tcc Ser 210															672
	ttt Phe															720

gga acc ctg gtc act gtc tcg agc tga Gly Thr Leu Val Thr Val Ser Ser 245 747

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Gly Ala Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu 35 40 45

Leu Ile Tyr Gly Ala Thr Ser Leu Gln Ser Gly Val Pro Ser Arg Phe 50 60

Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu 65 70 75 80

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Asn Val Leu Asn Thr 85 90 95

Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Gly 100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Gly Gly Gly Ser Gln Val 115 120 125

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val 130 135 140

Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Ser Asn Tyr Trp Ile 145 150 155 160

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Leu Ser Ser Leu 210		Glu Asp 215	Thr Ala	Val Tyr 220	Tyr Cys	Ala Aro	3
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							aag Lys 105					;	336
							tct Ser					:	384
							gtc Val					•	432
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	 	-	_	_			cag Gln	 _	_	 _	 		528
							gaa Glu 185					!	576
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Leu Ile Tyr Gly Ala Thr Asn Leu Ala Asp Gly Val Pro Ser Arg Phe 50 55 60

Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu 65 70 75 80

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Asn Val Leu Asn Thr 85 90 95

Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Gly 100 105 110

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val 115 120 125

Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val 130 135 140

Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Ser Asn Tyr Trp Ile 145 150 155 160

Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Glu 165 170 175

Ile Leu Pro Gly Ser Gly Ser Thr Glu Tyr Thr Glu Asn Phe Lys Asp 180 185 190

Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr Met Glu 195 200 205

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg 210 215 220

Tyr Phe Phe Gly Ser Ser Pro Asn Trp Tyr Phe Asp Val Trp Gly Gln 225 230 235 240

## Gly Thr Leu Val Thr Val Ser Ser 245

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		tac Tyr														1	92
		tcc Ser														2	:40
		gaa Glu														2	88
		act Thr														3	36
		ggt Gly 115														3	884
		gtg Val														4	32
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Lys Val Ser 145	Cys Lys	Ala Ser 150	Gly Tyr	Ile Ph 15		Asn Tyr	Trp	Ile 160	
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atc tta ccg Ile Leu Pro				Tyr Th					;
cgt gtt act Arg Val Thr 195					r Thr V				í
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tat ttt ttt Tyr Phe Phe 225					e Asp V				)
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Leu Ile Tyr		mb w Cow	Leu Gln	Ser Gl	v Val F	Pro Ser	Ara	Phe	
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<222> (1)..(744)

atg	gat		atg Met						48
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			gct Ala						288
			cag Gln						336
			ggc Gly						384
			ggc Gly						432
			gct Ala 150						480
			gcc Ala						528
			ggt Gly						576
			cgt Arg						624
			tcg Ser						672

tat ttt ttt ggt tct agc ccg aat tgg tat ttt gat gtt tgg ggt caa Tyr Phe Phe Gly Ser Ser Pro Asn Trp Tyr Phe Asp Val Trp Gly Gln 225 230 235 240	720
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Gly Ala Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu 35 40 45	
Leu Ile Tyr Gly Ala Thr Ser Leu Gln Ser Gly Val Pro Ser Arg Phe 50 55 60	
Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu 65 70 75 80	
Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Asn Val Leu Asn Thr 85 90 95	
Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Gly 100 105 110	ν.
Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gln Val 115 120 125	
Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val 130 135 140	

Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Ser Asn Tyr Trp Ile

Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Glu 165 170 175

Ile Leu Pro Gly Ser Gly Ser Thr Glu Tyr Thr Glu Asn Phe Lys Asp 180 185 190

Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr Met Glu
195 200 205

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg 210 215 220

Tyr Phe Phe Gly Ser Ser Pro Asn Trp Tyr Phe Asp Val Trp Gly Gln 225 230 235 240

Gly Thr Leu Val Thr Val Ser Ser 245